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Center for Neuroprosthetics

2013 ANNUAL REPORT

**Translational
Neural Engineering
Laboratory**

**Bertarelli Foundation
Chair in Cognitive
Neuroprosthetics**

**Bertarelli Foundation
Chair in
Neuroprosthetic
Technology**

**Defitech Foundation
Chair in Non-invasive
Brain-machine
Interface**

**Foundation IRP Chair
in Spinal Cord
Repair**

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Olaf Blanke

Stéphanie P. Lacour

José del R. Millán

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Foreword

Welcome to the Center for Neuroprosthetics

The 20th Century witnessed major advances in the investigation and understanding of the brain and its diseases. This culminated in the 1990s with the “decade of the brain”, which also saw the massive arrival of systems and cognitive neuroscience in humans based on the development of non-invasive brain imaging techniques. The field of neuroengineering also made breathtaking advances in biotechnology and microelectronics, as well as neural implants that make it possible to target specific regions in the brain, the spinal cord, and the peripheral nervous system for novel treatments. This acceleration and success in the neurosciences and neuroengineering was complemented by a third revolution: information technology and the birth of the digital age with major advances in computing power, e-health, and communication technologies.

The Center for Neuroprosthetics enthusiastically embraces these three revolutions and is establishing a truly interdisciplinary area of study for scientific discovery and neurotechnological design through cutting edge research in neuroscience, engineering, and computer science. To meet our ambitious translational goals in neuroprosthetics—that is, the repair and substitution of impaired sensory, motor and cognitive functions—we have over the last year further strengthened our strategic clinical partnerships with the University Hospitals in Geneva and Lausanne, the Swiss Rehabilitation Clinic in Sion, and Harvard Medical School.

The well-established treatments of deep brain stimulation for Parkinson’s disease, of cochlear implants for hearing loss, and of virtual reality for neuropsychiatric rehabilitation are just three of the success stories in this area. Clearly, much work lies ahead of us while we strive to provide enabling neurotechnological treatments to neurological and psychiatric patients.
Stay tuned.

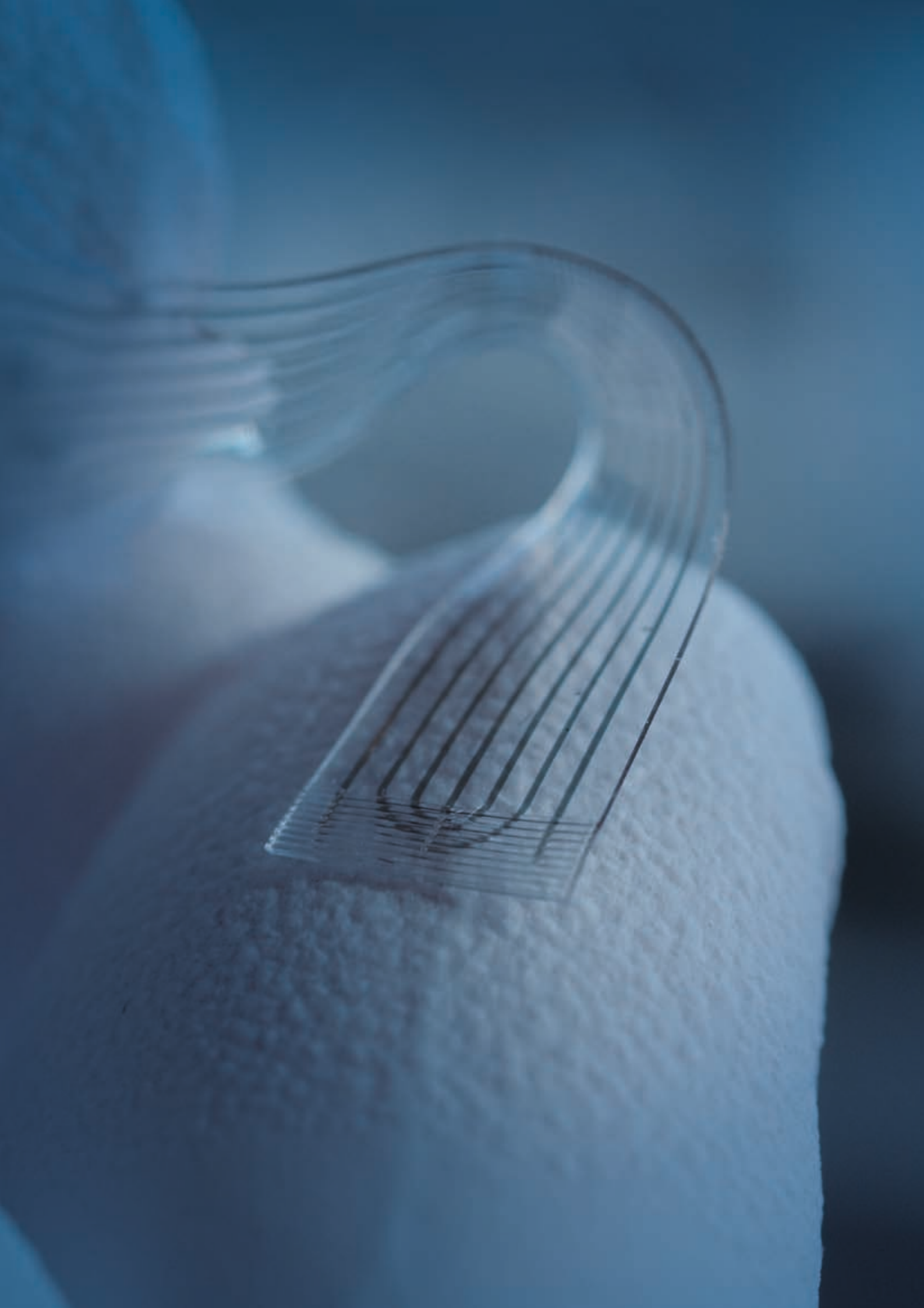
Olaf Blanke
Director of the Center for Neuroprosthetics
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Mission

The Center for Neuroprosthetics (CNP) capitalizes on its unique access to the advanced bio and neurotechnologies and state of the art brain research present at EPFL. We strive to develop new technologies that support, repair and replace functions of the nervous system. The development of such technologies or devices, called neuroprostheses, requires a fundamental understanding of the neurobiological mechanisms of the functions that should be replaced or repaired, for example sensory perception, cognitive operations or movement. It also requires technological capabilities to design novel devices, to record and process signals and to translate them into outputs that can command artificial limbs, bodies and robots, for motor function, or produce signals to activate the brain, in the case of sensory and cognitive prostheses.

The impact of neuroprosthetics for the treatment of sensory loss and impaired mobility has already been demonstrated. Over 200'000 people with impaired hearing have received cochlear implants and over 100'000 patients suffering from Parkinson's disease, movement disorders and clinical conditions such as drug-resistant depression and epilepsy, have been treated with deep brain stimulation and related techniques. With approximately a third of the population in Europe and the US afflicted by brain disorders, major advances in neuroprosthetics are necessary, including breakthroughs in cognitive neuroprosthetics for treating patients suffering from cognitive deficits such as those caused by Alzheimer's disease and vascular stroke.



Projects



Walk again

Movement intentions of a paralyzed rodent with spinal cord injury are decoded from real-time recording of brain activity. Decoded information is directly fed into a brain-spinal interface that computes optimal spinal cord stimulation patterns to execute the desired movement. As a result the animal is capable of locomotion and obstacle avoidance, even though the spinal cord motoneurons are physically separated from the brain.



Human-computer confluence

Robust real-time movement control of robots and wheelchair, pioneering work in virtual reality and brain-machine interface, and major advances in cognitive neuroscience and wearable technology are exploited to develop new devices and treatments for mobility restoration, analgesia, communication, neuroscience research, and entertainment.



Rehabilitation of upper limb sensorimotor loss

Merging insights from robotics and neuroengineering, our devices enable novel neurorehabilitation training for patients suffering from sensorimotor loss of the upper extremity. These tools are complemented by techniques from brain computer interfaces and virtual reality to further enhance rehabilitation outcomes for patients with sensorimotor loss, chronic pain and cognitive deficits.



Bionic hand

Biocompatible flexible electrodes are implanted into different peripheral arm nerves of amputee patients. Movement commands of the amputee patient are decoded from signals in the implanted electrodes and transmitted to the prosthetic hand, where they are translated into movements of the prosthetic hand and fingers. Signals from different sensors in the prosthetic hand can also be transmitted via the implanted electrodes to the peripheral nerve to enable sensory functions such as the sense of touch and of finger position. Novel non-invasive stimulation protocols are developed to enable touch and decrease phantom limb pain.

Walk again

Restoring sensorimotor functions after spinal cord injury

Robotic postural neuroprosthesis

Novel robotic postural neuroprosthesis to evaluate, enable, and train locomotion under natural walking conditions. The amount of support can be fine-tuned for each axis according to the animal's capacity.



Development of a brain-spinal interface to restore voluntary gait control after a spinal cord injury.



Soft microchannel electrode implant for monitoring afferent signals

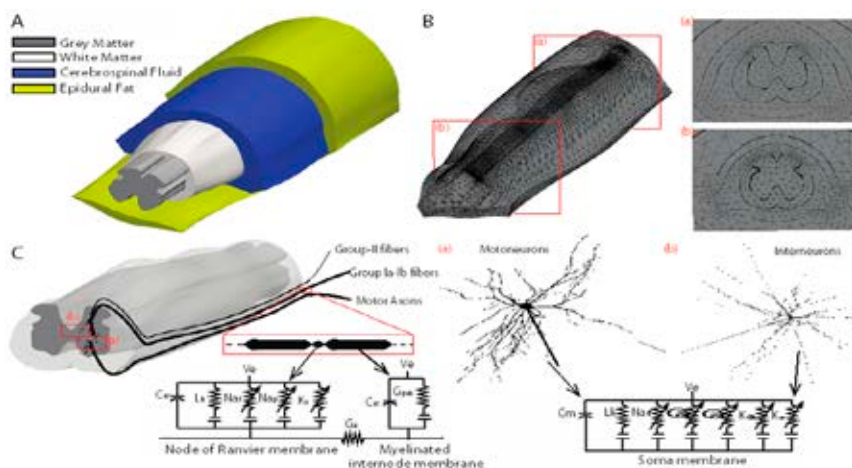
After spinal cord injury many patients do not only suffer from gait deficits, but also develop a neurogenic bladder characterized by the loss of voluntary control of micturition. In collaboration with scientists in the UK, we aim to design a closed-loop neuroprosthetic interface which can measure bladder fullness and prevent spontaneous voiding episodes without the necessity for surgical interventions.



A Computational Model for Epidural Electrical Stimulation of Spinal Sensorimotor Circuits

Spinal Neuroprosthetics and in particular epidural electrical stimulation (EES) of lumbosacral segments can restore a range of movements after spinal cord injury. However, the mechanisms and neural structures through which EES facilitates movement execution remain unclear. Researchers from the CNP developed a realistic finite element computer model of rat lumbosacral segments (A and B) to identify the currents generated by EES and coupled this model with an anatomically realistic biophysical model of sensorimotor circuits (C).

Our computational model, which we validated with actual measurements from the animal, offers an alternative to classical experimental approaches to optimize quickly and precisely the position, size, and configuration of EES electrodes.



The computational model: the realistic finite element model (A and B) and the coupled biophysical model of sensorimotor circuits.

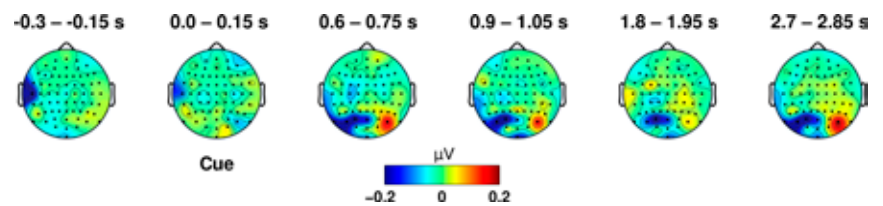
Human-computer confluence

Decoding brain activity for feeling and moving artificial bodies and robots



Cognitive signals for brain-computer interaction

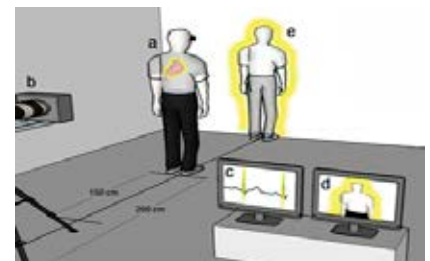
The operation of any neuroprosthetic device is modulated by the user's cognitive state, just as the control of our body is. These states reflect processes such as attention, body processing, and evaluation of information inflow generated by user's actions (e.g. erroneous decisions made by the neuroprosthesis). The figure shows the evolution of brain activity (8–14 Hz oscillations) while subjects covertly attend to their left or right visual field. The topographic maps represent the difference between the two conditions in six different time windows.



Modulating bodily self-consciousness with the heart

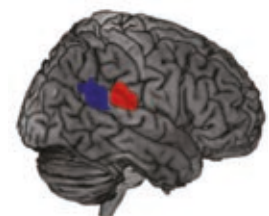
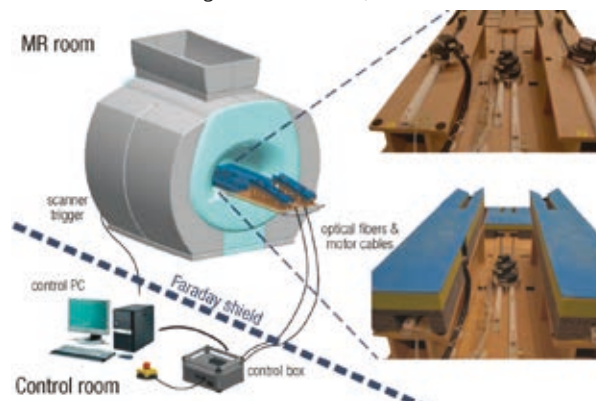
By projecting an interoceptive signal (the heartbeat) to the "skin" of an avatar that was seen by the participant through head-mounted displays we modulated several conscious bodily feelings (body ownership and self-awareness). Our data show that the brain integrates physiological signals from the inside of the body with those from the outside of the body (i.e. visual or tactile signals). The analgesic potential of modified versions of this paradigm are now explored in several clinical populations suffering from chronic pain.

Brain-based neuroprostheses that decode movement intentions and embody robotic and virtual devices.



Neuroscience, robotics and haptics: the brain mechanisms of feeling a virtual and robotic body as your own

Custom made robotic devices allow us to control a vast array of multisensory stimulations for the induction of embodiment and pain reduction during fMRI acquisition (including EPFL's ultra-high 7T MR-scanner).



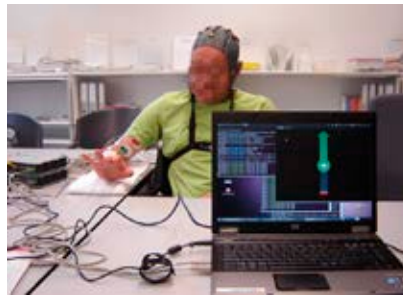
Temporo-parietal activity reflects the experience of embodiment (red). If the same area is damaged (blue), neurological patients have impairments in embodiment. The area's implication in pain treatments is currently explored.

Rehabilitation of upper limb sensorimotor loss

Providing neuro-technological tools for cerebral stroke rehabilitation

Brain-computer interfaces and rehabilitation

Brain-computer interfaces (BCI) can help stroke patients to regain motor control of their paralyzed hand. The BCI detects the patient's intent to execute a hand extension movement and activates appropriate functional electrical stimulation patterns to activate the hand muscles and execute the desired action. The BCI also checks that intent is encoded in physiologically relevant cortical areas and frequencies.



Stroke rehabilitation via hybrid devices.

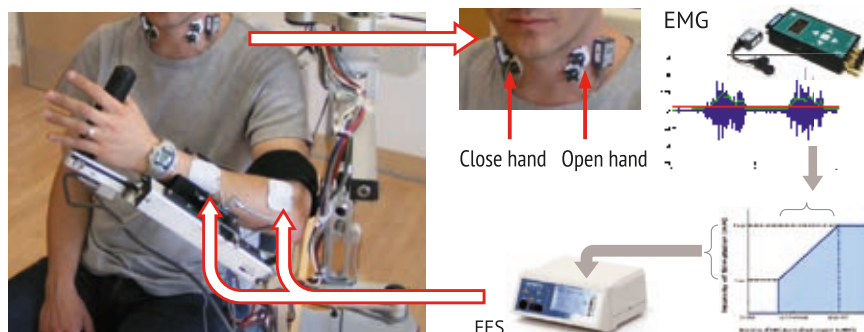
Precise neuro-muscular electrical stimulation of hand and fingers

Our electrode arrays facilitate specific flexion and extension of the fingers and also control the wrist.



Hybrid tools for reaching and grasping rehabilitation

The system consists of a passive upper arm exoskeleton with gravity compensation, a 4-channel functional electrical stimulator (FES) and a wireless surface electromyographic system (EMG). The user controls the opening and closing of his/her own hand by selective activation of neck muscles (left and right sternocleidomastoid).



Virtual reality for pain treatment

New systems based on neuroscientific theories of bodily self-consciousness and using virtual reality technologies have now been developed for chronic pain patients (amputation, cerebral stroke or orthopedic disorders).



Bionic hand

Restoring sensory and motor functions after arm or hand amputation

Restoring natural sensory feedback for real-time bidirectional robotic arm control in a human amputee

The ideal bidirectional hand prosthesis should involve both a reliable decoding of the user's intentions and the delivery of sensory feedback through the remnant afferent pathways simultaneously and in real time. We showed that, by stimulating peripheral nerves using intraneural electrodes, natural sensory information can be provided to an amputee during the real time control of a hand prosthesis. This feedback enabled the participant to effectively modulate the grasping force of the prosthesis without any visual or auditory feedback.

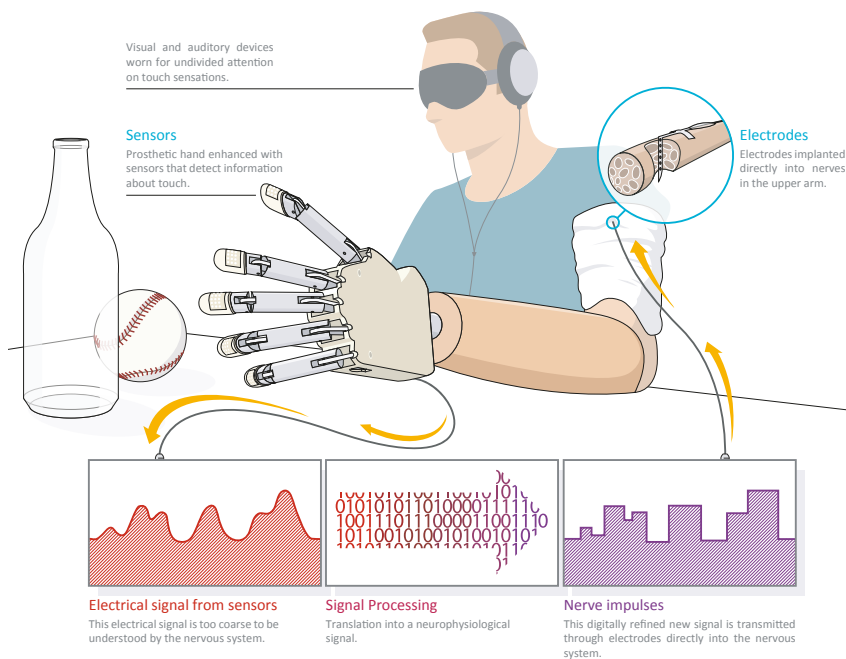
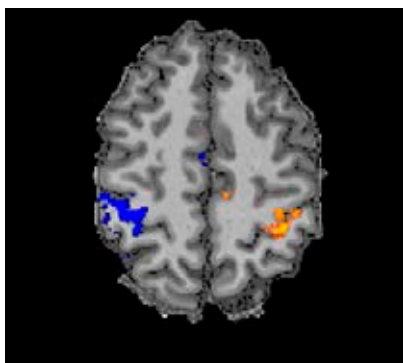
Results also show that by restoring dynamic sensory information derived from specific hand locations, a higher complexity of perception can be obtained, allowing the subject to identify the compliance and shape of different objects.

Connecting a bionic arm directly to the peripheral nervous system of the arm.



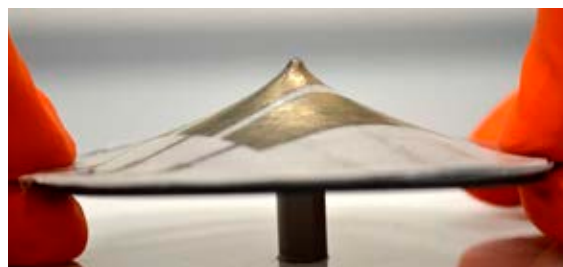
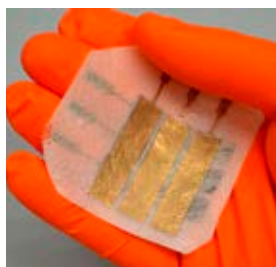
Neural representation of the phantom hand in a human amputee with targeted muscle reinnervation

Targeted muscle reinnervation (TMR) interfaces persisting nerves from the amputated limb with another muscle of the amputee (here the chest muscle) allowing for control of a robotic or prosthetic limb. In collaboration with scientists in the US, we used ultra-high resolution imaging at 7 tesla fMRI and showed that the cortical hand motor centers in such TMR patients were restored to the location of the hand motor centers controlling the non-amputated hand. This differs from the location of motor centers in amputee patients without TMR and will benefit the design of future neuroprostheses.



Highly deformable pressure sensors microfabricated on soft polyurethane foam

Future prosthesis may be covered with artificial skin. Our artificial skin can sustain crumpling as well as sharp indentation while the gold film coating remains intact.





Laboratories

Micera Lab

Translational Neural Engineering Laboratory

<http://tne.epfl.ch>

Blanke Lab

Bertarelli Foundation Chair in Cognitive Neuroprosthetics

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Lacour Lab

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Silvestro Micera

Bio

Silvestro Micera is Director of the Translational Neural Engineering Laboratory at the Center for Neuroprosthetics and the Institute of Bioengineering. He received the University degree (Laurea) in Electrical Engineering from the University of Pisa, in 1996, and the Ph.D. degree in Biomedical Engineering from the Scuola Superiore Sant'Anna, in 2000. In 2009 he was the recipient of the "Early Career Achievement Award" of the IEEE Engineering in Medicine and Biology Society.

Dr. Micera's research interests include the development of neuroprostheses based on the use of implantable neural interfaces with the central and peripheral nervous systems to restore sensory and motor function in disabled persons.

Results Obtained in 2013

In 2013, we performed our second implant of intraneural electrodes in Rome. This new experiment showed, for the first time, the possibility to develop a real-time bidirectional control of hand prostheses using intraneural peripheral electrodes. The paper has been published in Science Translational Medicine.

We were also deeply involved in the activities led by Professor Courtine's team to develop a novel neuroprosthesis to restore locomotion using epidural electrical stimulation (EES). This activity produced a publication in the Journal of Neuroscience on advanced modeling for the understanding of EES basic mechanisms, a review paper published in Science Translational Medicine and other papers submitted or in preparation. On this topic we are responsible for the development of novel models to better understand EES, of novel control strategies to improve the performance of EES, and of several experiments to characterize cortical activities using intracortical electrodes during locomotion.

We are also currently working with the University Hospital of Geneva (Prof. Guyot) to develop and validate a novel neuroprosthesis to restore vestibular functions in disabled subjects. The TNE is responsible for the integration of the device, and the development of novel approaches to assess the performance of this device and collaborates on the clinical and neurophysiological characterization together with HUG clinical team. We are also starting a new industrial collaboration on this topic.

Finally, we developed a wearable system for functional electrical stimulation to restore grasping in highly disabled subjects. The system is currently in clinical testing in Italy.

Keywords

Implantable neuroprostheses; rehabilitation robotics; wearable devices; neuro-controlled artificial limbs; reaching and grasping; locomotion; functional electrical stimulation.

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Selected Publications

Spalletti C, Lai S, Mainardi M, Panarese A, Ghionzoli A, Alia C, Gianfranceschi L, Chisari C, Micera S, Caleo M (2014). A robotic system for quantitative assessment and poststroke training of forelimb retraction in mice. *Neurorehabilitation and Neural Repair*, 2:188-96.

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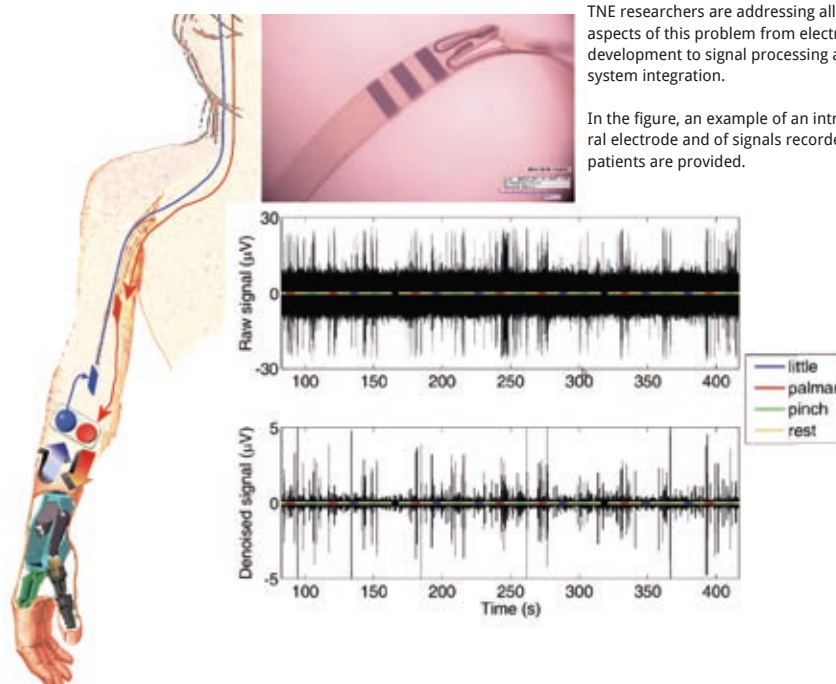
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The TNE lab is working on the development of a novel bionic hand controlled by the peripheral nervous system. The TNE researchers are addressing all the aspects of this problem from electrode development to signal processing and system integration.

In the figure, an example of an intraneural electrode and of signals recorded in a patients are provided.



Blanke Lab

<http://Inco.epfl.ch>



Olaf Blanke

Bio

Olaf Blanke is founding director of the Center for Neuroprosthetics at the Ecole Polytechnique Fédérale de Lausanne (EPFL), holds the Bertarelli Foundation Chair in Cognitive Neuroprosthetics, and is Professor of Neurology at the Department of Clinical Neurosciences at Geneva University Hospital. In his research, he applies paradigms from neuroscience, neuroimaging, cognitive science, robotics, and virtual reality in healthy subjects, neurological and psychiatric patients, patients suffering from chronic pain, to understand and modulate body and motor representations in the human brain, to develop a neurobiological model of self-consciousness, and to apply these findings in cognitive neuroprosthetics and neurorehabilitation.

Results Obtained in 2013

Research highlights clustered around three topics: (1) physiological and behavioral mechanisms of bodily self-consciousness using virtual reality, (2) the brain mechanisms of bodily self-consciousness in temporo-parietal and insular cortex, and (3) the translation of this knowledge to robotics and sensory substitution. First, in a series of studies we showed that interoceptive (e.g. cardiac) signals are powerful modulators of bodily self-consciousness (Aspell et al., 2013) and that vestibular signals strongly contribute to self-consciousness (Pfeiffer et al., 2013). Such experimentally-induced changes in bodily self-consciousness also impact physiological states of the body - such as body temperature control (Salomon et al., 2013) and pain regulation (Romano et al., 2014) - and even social experience and perception (Teneggi et al., 2013). Second, using functional magnetic resonance we quantified the extended bilateral cortical network of bodily self-consciousness that causes these changes; the network included temporo-parietal cortex, insular cortex, and supplementary motor area (Ionta et al., 2014; figure B), further confirmed in a large study in neurological patients with focal brain damage (Heydrich and Blanke, 2013; figure C). Third, by combining haptics, robotics, virtual reality and cognitive science, we investigated how bodily self-consciousness extends to robotic tools (Sengül et al., 2012), can be modulated by haptic devices (figure A), and extends to virtual replacements of the body by recruiting neural mechanisms of motor imagery (Evans and Blanke, 2013). We also showed that surgical robotic devices used during minimally-invasive operations need to provide congruent visuo-tactile information (Rognini et al 2013), force feedback and well-defined haptic signals (Sengül et al., 2013), in order to boost user performance, control, and embodiment.

Keywords

Multisensory integration, sensorimotor, neuroscience robotics, perception, neuroprosthetics, temporo-parietal cortex, bodily awareness, self-consciousness, self-location, first-person perspective, neuroimaging, fMRI, EEG, neuropsychology, cognitive neuroscience, substitution, neurology, virtual reality, vestibular system, brain-computer interfaces.

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Selected Publications

Romano D, Pfeiffer C, Maravita A, Blanke O (2014). Illusory self-identification with an avatar reduces arousal responses to painful stimuli. *Behavioural Brain Research* 261:275-281.

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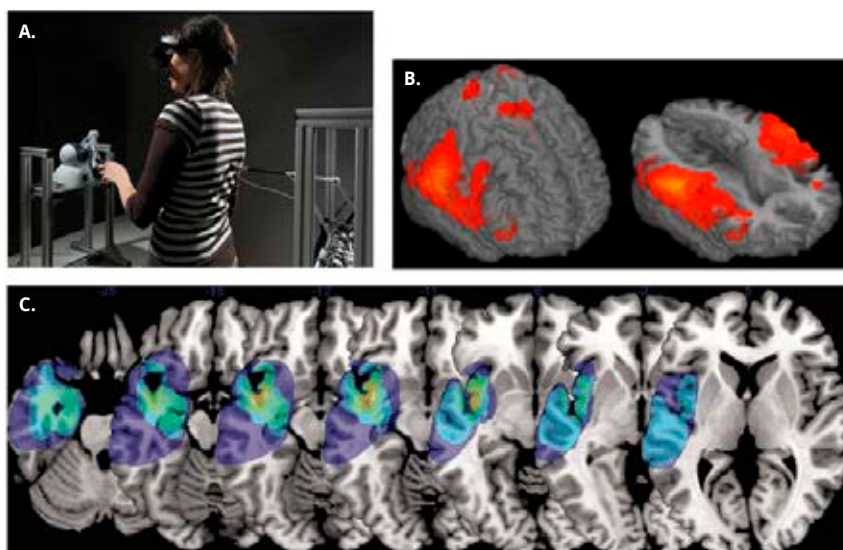
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A. Experimental robotic setup for sensorimotor processing, bodily self-consciousness, and psychiatry.

B. The brain network that mediates the induction of embodiment for an avatar, including temporo-parietal cortex, insular cortex, and the supplementary motor area.

C. Location of brain damage in neurological patient leading to abnormal embodiment (note the overlap with the insula also described for embodiment in healthy subjects; figure B).

Lacour Lab

<http://lsbi.epfl.ch>



Stéphanie P. Lacour

Bio

Prof. Stéphanie P. Lacour holds the Bertarelli Foundation Chair in Neuroprosthetic Technology at the School of Engineering at the Ecole Polytechnique Fédérale de Lausanne. She received her PhD in Electrical Engineering from INSA de Lyon, France, and completed postdoctoral research at Princeton University (USA) and at the University of Cambridge (UK). Her research focuses on the materials, technology and integration of soft bioelectronic interfaces including artificial skin, ultra-compliant neural electrodes for in vitro platforms as well as in vivo implants.

The Laboratory for Soft Bioelectronics Interfaces (LSBI) explores how to design and manufacture man-made electronic platforms with mechanical properties adapted to those of the host biological tissues so that minimal perturbation is induced in vivo and/or truly wearable systems become possible. Envisioned applications include assistive technologies for patients with impaired nerves or spinal cord injuries in the form of soft implantable electrodes, and wearable interfaces in skin-like formats for prosthetic sensory skins. We use fabrication methods borrowed from the microelectronics and MEMS industry and adapted to soft substrates like elastomers. We develop novel characterization tools adapted to mechanically compliant bioelectronic circuits. Moving soft bioelectronics forward requires innovation in the fields of materials, technology, engineering, and biocompatibility, and a multidisciplinary mindset.

Results Obtained in 2013

Tactile sensory skin

In 2013, the LSBI developed advanced technologies for creating robust multilayer stretchable electronics using thin films on elastomeric polymers. Two key developments were stretchable vias that link electrical traces on stacked layers of materials and a technique for creating reliable electrical interconnects between soft and rigid materials. These techniques allowed for manufacturing porous foam capacitive tactile sensors that have greatly improved sensitivities over similar sensors of bulk material. The 'stretchability' of the sensors makes them especially attractive for manipulation tasks which require the sensors to flex and stretch. These sensors are currently being implemented on multiple robotic manipulators to provide tactile feedback.

We have also developed a reliable process for fabricating high-performance thin-film transistors (TFTs) with Indium Gallium Zinc Oxide (IGZO) channels. Integration of these devices with the pressure microsensors on soft substrates, will form a versatile platform for tactile monitoring by an artificial skin.

Polymeric neural interfaces

In 2013, we have developed a range of electrode to interface both the central and peripheral nervous systems.

2013 was dedicated to testing in-vivo a chronic spinal cord stimulator implant. We demonstrated high specificity of stimulation in sub-dural implanted rats with low stimulation currents. In addition to electrical stimulation, the use of elastomer microfabrication technology enabled us to incorporate a microfluidic system to deliver drugs. We used the electrochemical array in rat spinal cord injury models where we combined electrical and chemical stimulation, and training, to regain stepping.

We have also optimised the design and fabrication of a soft, nerve-like regenerative implant. The microchannel electrode implants have supported nerve re-growth up to nine months after implantation and yielded very promising electrical recordings showing neural activity on awake and freely moving animals.

Keywords

Microelectrode arrays, neural interfaces, stretchability, sensory neurons, neuro prosthesis, tactile sensors, polymers, thin films, biocompatibility, thin film electronics, micro nanofabrication.

Team

Assistant Professor

Stéphanie P. Lacour

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Aaron Gerratt

Tero Kulmala

Ivan Minev

Kate Musick

PhD students

Amelie Guex

Arthur Hirsch

Hadrien Michaud

Cedric Paulou

Alessia Romeo

Administrative Assistant

Carole Weissenberger

Selected Publications

Gux A, Joris P, Slama M, Brown C, Renaud P, Lee DJ, Lacour SP (2013). Microfabricated auditory brainstem implants on polyimide film. Proc. of the 6th IEEE EMBS conference on Neural Engineering, paper 600, San Diego 2013.

Musick K, Chew DJ, Fawcett JW, Lacour SP (2013). PDMS regenerative peripheral nerve interfaces. Proc. of the 6th IEEE EMBS conference on Neural Engineering, paper 14, San Diego 2013.

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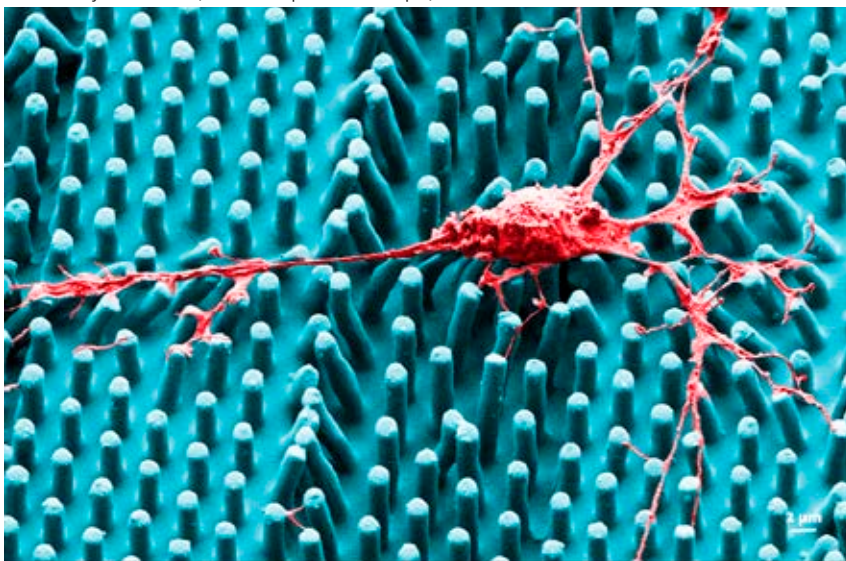
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FitzGerald JJ, Lago N, Benmerah S, Serra J, Watling CP, Cameron RE, Tarte E, Lacour SP, McMahon SB and Fawcett JW (2012). A regenerative microchannel neural interface for recording from and stimulating peripheral axons in vivo. Journal of Neural Engineering 9:016010.

Scanning electron microscopy image of a neuron spreading on an artificially soft surface. (scale : micropost diameter 2µm).



Millán Lab

<http://cnbi.epfl.ch>



José del R. Millán

Bio

Prof. José del R. Millán holds the Defitech Chair at the École Polytechnique Fédérale de Lausanne (EPFL) where he explores the use of brain signals for multimodal interaction and, in particular, the development of non-invasive brain-controlled robots and neuroprostheses. In this multidisciplinary research effort, Dr. Millán is bringing together his pioneering work in the fields of brain-computer interfaces and adaptive intelligent robotics. His research on brain-computer interfaces was nominated finalist of the European Descartes Prize 2001 and he has been named Research Leader 2004 by the journal *Scientific American* for his work on brain-controlled robots. He is the recipient of the IEEE Norbert Wiener Award 2011 for his seminal and pioneering contributions to non-invasive brain-computer interfaces. The journal *Science* has reviewed his work as one of the world's key researchers in the field of brain-computer interfaces. Dr. Millán is the coordinator of a number of European projects on brain-computer interfaces and also is a frequent keynote speaker at international meetings. His work on brain-computer interfaces has received wide scientific and media coverage around the world.

Results Obtained in 2013

We have explored two major research directions this year that revolve around the design and testing of brain-computer interface (BCI) principles for replacing lost motor functions and for enhancing interaction experiences.

In the former case, motor-impaired users have demonstrated the effectiveness of our brain-controlled devices, which are based on the voluntary, spontaneous modulation of EEG rhythms associated to imagination of motor tasks (Leeb et al., 2013a). Our work with patients has also been extended to stroke rehabilitation (Biasiucci et al., 2013).

BCI applications extend beyond disabled users, as it has the potential to augment the interaction experience by providing additional information associated to brain correlates of volitional cognitive processes. We are interested in decoding some of these processes during both covert behavior (non-observable action) and while the user is undertaking natural actions such as eye movements to scan a scene or body movements to drive a car. In particular, we have investigated visual cognitive processes (Tonin et al., 2013; Ušćumlić et al., 2013) and how to predict driver's actions before they occur (Zhang et al., 2013; Gheorghe et al., 2013).

Finally, we have conducted basic studies aiming at improving the underlying pattern recognition (Chavarriaga et al., 2013a; Sagha et al. 2013) and brain signal processing (Garipelli et al., 2013) techniques. In parallel, we have developed new components to facilitate learning of brain control and operation of devices, such as hybrid BMI (Carlson et al., 2013), tactile feedback (Leeb et al., 2013b), shared-control architectures (Carlson and Millán, 2013), muscle synergies (Beuchat et al., 2013), and the use of transcranial direct current stimulation (Chavarriaga et al., 2013b).



Keywords

Brain-computer interfaces, Neuroprosthetics, Statistical machine learning, Human-robot interaction, Adaptive robotics, Neuroscience, EEG, Local field potentials.

Team

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Najate Gechoul

Selected Publications

Carlson TE and Millán JdR (2013). Brain-Controlled wheelchairs: A robotic architecture. *IEEE Robotics and Automation Magazine*, 20(1):65–73.

Leeb R, Perdakis S, Tonin L, Biasiucci A, Tavella M, Molina A, Al-Khodairy A, Carlson T, and Millán JdR (2013a). Transferring brain-computer interfaces beyond the laboratory: Successful application control for motor-disabled users. *Artificial Intelligence in Medicine*, 59(2):121–132.

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Biasiucci A, Leeb R, Al-Khodairy A, Buhlmann V, and Millán JdR (2013). Motor recovery after stroke by means of BCI-guided functional electrical stimulation. 5th International BCI Meeting. Asilomar (CA), USA.

A volunteer drives our car simulator while simultaneously recording electroencephalogram (EEG) signals. The experimental setup allows synchronized recordings of car actions (steering angles, pedals position), EEG and other physiological signals from the driver (electrooculogram, EOG, and electromyogram, EMG).



Courtine Lab

<http://courtine-lab.epfl.ch>



Grégoire Courtine

Bio

Grégoire Courtine was trained in Mathematics and Physics, but received his PhD in Experimental Medicine from the Inserm Plasticity and Repair, France, in 2003. After a Post-doctoral training in Los Angeles (UCLA), he established his own laboratory at the University of Zurich in 2008. In December 2011, he accepted the International paraplegic foundation (IRP) chair in spinal cord repair at the Center for Neuroprosthetics at the EPFL. He received numerous honors such as the UCLA Chancellor's award, the Schellenberg Prize for his advances in spinal cord repair, the 2013 Debiopharm prize, and a fellowship from the European Research Council (ERC). His works has received substantial coverage in the national and international media.

The World Health Organization estimates that as many as 500'000 people suffer from a spinal cord injury (SCI) each year. Our goal is to elaborate innovative interventions that improve the recovery of motor functions in animal models of SCI, and to translate these discoveries into effective therapies to ameliorate the quality of life of injured people. To achieve this goal, we are developing a range of neuroprosthetic technologies combining pharmacological and electrical neuromodulation therapies of the brain, brainstem, and spinal cord. The underlying objective of these interventions is to tap into preserved neuronal circuits after injury to promote functional states. We leverage these neuroprosthetic interventions to boost activity-dependent remodeling of brain and spinal circuits during robot-assisted neurorehabilitation procedures. Finally, we apply neuroregenerative interventions integrating neural stem cells into growth factor filled hydrogels to create a growth permissive environment during rehabilitation.

Our general strategy consists of uncovering mechanisms in genetically modified mice, optimizing interventions in rat models, ensuring the safe and efficacious translation of these procedures in non-human primates, and finally evaluating these therapies in clinical trials.

Results Obtained in 2013

During this past year, we achieved significant breakthroughs along 4 parallel, but highly interactive research fronts:

Mechanistic studies in genetically modified mice

We exploited mice with specific genetic mutations to uncover the mechanisms through which noradrenergic replacement therapies improve motor control after SCI. This patented work identified novel pharmacological targets to facilitate rehabilitation in paraplegic patients. We also established a robotic platform for optogenetic studies in mice. We expressed light-activated channels in cortical neurons to demonstrate the ability of motor cortex input to modulate electrochemically-enabled locomotion in mice with severe SCI.

Neuroprosthetic technologies in rats

We developed neural interfaces to deliver multisite chemical and electrical stimulations to the spinal cord. To manipulate stimulation patterns in real-time, we elaborated a platform interfacing biomechanical states (feedback) with control policies (feed-forward). Closed-loop control of multisite spinal cord stimulation allowed paralyzed rats to climb staircases of various lengths and heights with remarkable fluidity. These control policies will directly be tested in paraplegic patients.

Translational research platform in monkeys

We established a translational platform for natural whole-body motion in monkeys, where motor cortex and muscle activity is recorded wirelessly and in broad-band, and whole-body kinematics are measured through high-precision video reporting. These signals are interfaced wirelessly with an implanted pulse generator that can deliver stimulations in the brain and spinal cord. This translational platform will allow us to optimize safety and efficacy of our interventions prior to clinical applications.

Clinical research in paraplegic patients

In collaboration with Dr Jocelyne Bloch, who supervises the functional neurosurgery program at the CHUV, we prepared a clinical study to investigate the efficacy of robot-assisted gait rehabilitation enabled by electrical spinal cord stimulation to improve the recovery of locomotion in paraplegic people. For this, we translated all the technology developed in rodents into a newly-renovated gait rehabilitation platform at the CHUV. A Clinical Investigation Protocol has been positively reviewed by the local ethical committee.

We anticipate that 2014 will be a year full of new and exciting discoveries.

Keywords

Spinal cord injury, repair, neurorehabilitation, neuroprosthetics, neuroregeneration, stem cell, brain-machine interface, neuromodulation, , robotic, neuronal recordings, optogenetic, EMG, kinematic, locomotion, neuromorphology, mice, rats, monkeys, humans.



Team

Associate Professor
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Nikolaus Wenger (MD PhD candidate)

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Joachim von Zitzewitz

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Pierre-Yves Helleboid
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Hugo Hoedemaker
JuneSeung Lee
Camille Le Goff
Jenifer Miehlsbradt
Audrey Nguyen
Solange Richter
Giorgio Ulrich

Selected Publications

Borton D, Micera S, Millán J del R, Courtine G. (2013). Personalized neuroprosthetics. *Science Translational Medicine*, 5:210.

Beuparlant J, van den Brand R, Barraud Q, Friedli L, Musienko P, Dietz V, Courtine G (2013) Undirected compensatory plasticity contributes to neuronal dysfunction after severe spinal cord injury. *Brain* 136:3347-3361.

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Courtine G, Micera S, Digiovanna Millán JdR (2013). Brain-machine interface: closer to therapeutic reality? *The Lancet* 381:515-7.

Horst M, Heutschi J, van den Brand R, Andersson KE, Gobet R, Sulser T, Courtine G, Eberli D (2013). Multisystem Neuroprosthetic Training Improves Bladder Function After Severe Spinal Cord Injury. *Journal of Urology* 189:747-53.

Musienko PE, Gorski OV, Kilimnik VA, Kozlovskaya IB, Courtine G, Edgerton VR, Gerasimenko YP (2013). Neuronal control of posture and locomotion in decerebrated and spinalized animals. *Rossiiskii fiziologicheskii zhurnal imeni I.M. Sechenova* 99:392-405.

Van den Brand R, Heutschi J, Barraud Q, Digiovanna J, Bartholdi K, Huelimann M, Friedli L, Vollenweider I, Martin Moraud E, Duis S, Dominici N, Micera S, Musienko PE, Courtine G (2012). Restoring voluntary control of locomotion after paralyzing spinal cord injury. *Science* 336(6085): 1182-1185

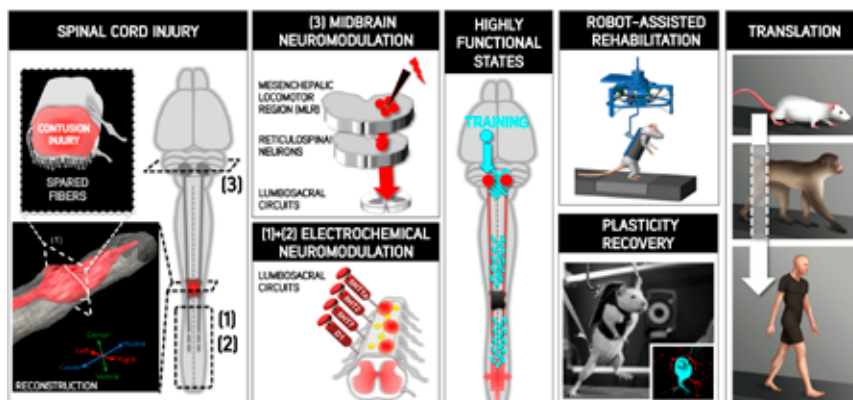
Dominici N, Keller U, Vallery H, Friedli L, van den Brand R, Starkey ML, Musienko P, Riener R, Courtine G (2012). Novel robotic interface to evaluate, enable, and train locomotion and balance after neuromotor disorders. *Nature Medicine* 18:1142-1147.

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Musienko P, Courtine G, Tibbs JE, Kilimnik V, Savochin A, Garfinkel A, Roy RR, Edgerton VR, Gerasimenko Y (2012). Somatosensory control of balance during locomotion in decerebrated cat. *Journal of Neurophysiology* 107:2072-2082.

Nout YS, Rosenzweig ES, Brock JH, Strand SC, Moseanko R, Hawbecker S, Zdunowski S, Nielson JL, Roy RR, Courtine G, Ferguson AR, Edgerton VR, Beattie MS, Bresnahan JC, Tuszynski MH (2012). Animal models of neurologic disorders: a nonhuman primate model of spinal cord injury. *Neurotherapeutics* 9:380-392.

We developed clinically relevant animal models of spinal cord injury. To enable functional states, we apply chemical and electrical neuromodulation therapies of the brainstem (3) and spinal cord (2, 3). These interventions boost plasticity during robot-assisted gait training, promoting recovery of voluntary locomotion in paralyzed rats. These interventions are gradually translated into clinical applications.



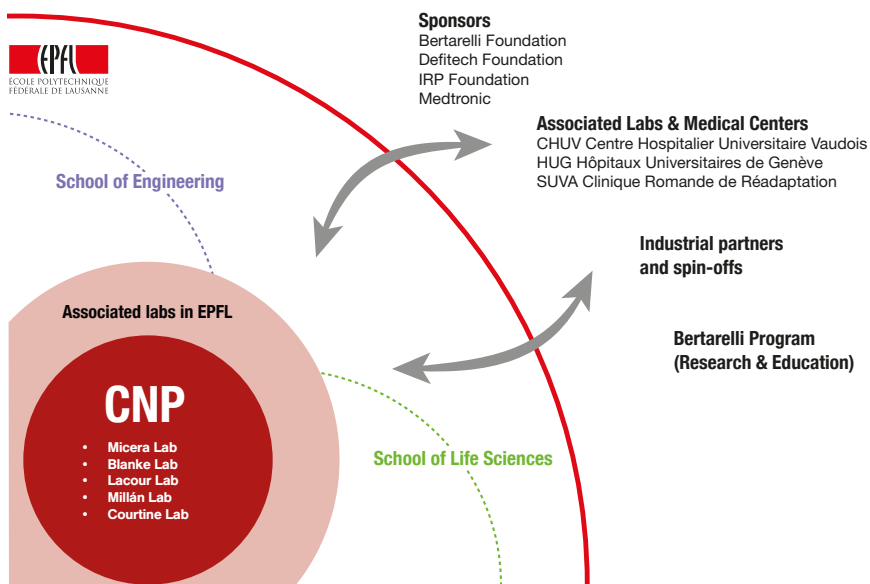


Partners and activities

The Center for Neuroprosthetics draws upon EPFL's expertise in biology, neuroscience, brain imaging, and genetics as well as biomedical, electrical, mechanical engineering, micro- and nanotechnology. The Center will also draw upon EPFL's cutting edge research in signal analysis, theoretical and computational neuroscience, the recently launched European Flagship "Human Brain Project" and the Swiss National Center of Competence in Research in "Robotics" and Psychiatric diseases ("Synapsy").

Partners

The Center for Neuroprosthetics is part of the School of Life Sciences and the School of Engineering. In addition, through support from the Bertarelli foundation, a new research collaboration - dedicated to translational neuroscience and neuroengineering has been created between Harvard Medical School, EPFL's Institutes of Bioengineering and Neuroscience, and the Center for Neuroprosthetics.



Associated laboratories

AMINIAN Kamiar, Laboratory of Movement Analysis and Measurement (EPFL)

BLEULER Hannes, Robotic Systems Laboratory (EPFL)

BLOCH Jocelyne, Stereotactic and Functional Neurosurgery Program, Department of Neurosurgery (CHUV)

BOULIC Ronan, Immersive Interaction Group (EPFL)

DERIAZ Olivier, Rehabilitation & Readaptation Research Institute (Sion)

JANSSENS Jean-Paul, ADLER Dan, HERITIER BARRAS Anne-Chantal, IANCU FERFOGLIA Ruxandra, Center for amyotrophic lateral sclerosis, Department of Pneumology and Neurology (HUG)

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MURRAY Micah, IONTA Silvio, Laboratory for Investigative Neurophysiology (CHUV)

PAIK Jamie, Reconfigurable Robotics Laboratory (EPFL)

RAFFOUL Wassim, Department of Plastic and Reconstructive Surgery (CHUV)

SCHNIDER Armin, GUGGISBERG Adrian, PTAK Radek, Cognitive Neuro-Rehabilitation Laboratory, Neurorehabilitation Clinic (HUG)

SEECK Margitta, EEG and Epilepsy unit, Department of Neurology (HUG)

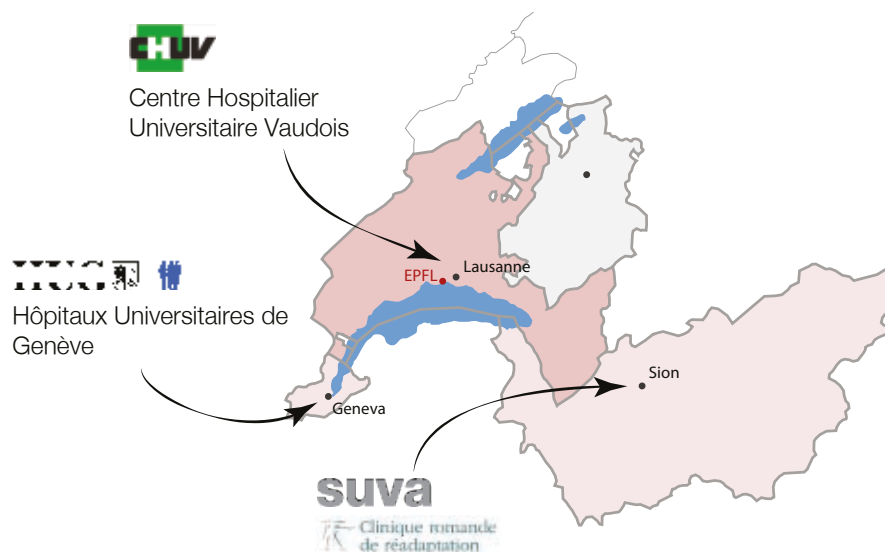
SCHALLER Karl, MOMJIAN Shahan, Department of Neurosurgery (HUG)

VAN DE VILLE Dimitri, Medical Image Processing Laboratory (EPFL)

VUADENS Philippe, RIVIER Gilles, Readaptation Clinic (SUVA)

Associated medical centers

The Center for Neuroprosthetics has strategic partnerships with Geneva University Hospital (Hôpitaux Universitaires de Genève, HUG), Lausanne University Hospital (Centre Hospitalier Universitaire Vaudois, CHUV), and the Swiss Rehabilitation Clinic in Sion (Clinique Romande de Réadaptation, CRR), as well as with the regional biomedical industry.





Swiss Rehabilitation Clinique, SUVA and EPFL-Valais-Wallis

Since October 2013, five EPFL clinician-researchers are working in collaboration with the research teams of Dr Vuadens, Dr Rivier, and Dr Dériaz at the Swiss Rehabilitation Clinic in Sion (Clinique Romande de réadaptation CRR). The research is funded within the framework of an intensified collaboration between the canton of Valais and the EPFL. The mission of the CNP-Valais Team is to conduct clinical and neuroengineering research to validate and further improve the effectiveness of the innovative healthcare technologies created and developed at the CNP. The picture shows Robert Leeb (Biomedical engineer), Dragana Viceic (Neurologist), Aurélie Bouzerda-Wahlen (Neuropsychologist), Michela Bassolino (Neuropsychologist) and Thomas Schmidlin (Physiotherapist) on the new CNP site in Sion. The CNP projects currently focus on stroke rehabilitation, brain-computer interfaces, pain, and locomotion. The next phase of this intensive clinical and research collaboration will be the creation of a new EPFL-Valais-Wallis professorship in Sion.



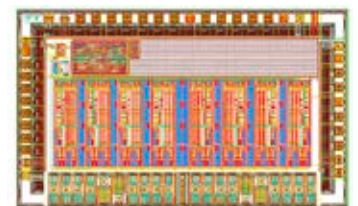
Department of Neurosurgery, CHUV and EPFL-Valais-Wallis

Together with the neurosurgery department at CHUV, the Courtine Lab designed an advanced gait rehabilitation platform. A room located in the neurorehabilitation unit at the Nestlé Rehabilitation Hospital has been entirely renovated to integrate the most advanced technologies for the recordings and rehabilitation of people with locomotor impairments. In collaboration with pivotal players in the Department of Clinical Neurosciences at the CHUV, in particular the functional neurosurgeon Dr Jocelyne Bloch, the CNP is preparing a clinical trial to evaluate the efficacy of robot-assisted rehabilitation enabled by electrical spinal cord stimulation to improve the recovery of locomotion in people with spinal cord injury. This collaboration will foster further interactions with the CHUV and the hospitals in Sion to achieve the translation of EPFL technologies into neuroprosthetic treatments to improve the quality of life of people with neurological disorders.



Department of Neurosurgery, HUG and UNIGE

In partnership with the neurosurgery department of the University Hospital of Geneva (Prof. Karl Schaller), the CNP is developing a wireless neural implant for cortical stimulation and recording in patients with cerebral stroke or tumors. The project involves the groups of Professors Yusuf Leblebici and Philippe Renaud and at CNP those of Professors Stéphanie Lacour, Olaf Blanke and José del R. Millán.



Selected highlights

January 2013

When the mind controls machines

Three presentations took place in Sion during the closing seminar of the TOBI European research program, which has been coordinated by CNP's José del R. Millán, holder of the Defitech Foundation Chair in Non-Invasive Brain-Machine Interface. More than hundred patients suffering from severe motor impairments have benefitted from the development of non-invasive brain-machine interfaces for rehabilitation.



April 2013

TEDMED Live Bologna

Well-received seminar on neuroprosthetics and bionics by Silvestro Micera at the prestigious TEDMED event in Bologna, Italy. The seminar was entitled "Developing a bionic prosthesis that allows to perceive touch".



June 2013

Air bubbles could be the secret to artificial skin

How can you turn a material that is essentially rigid and breakable into something that is flexible and can bend? Stéphanie Lacour made a major step forward and published her research published in the journal *Advanced Materials*.

CNP researcher at TEDGlobal 2013

Grégoire Courtine presented his latest findings for the revolutionary treatment of spinal cord injury in Edinburgh, Scotland.

July 2013

Body illusion cools down physical body

Researchers from the Blanke Lab show that the feeling to be immersed with a virtual body -- an "avatar" -- is associated with a drop in temperature monitoring of the participant's own body. The paper was published in the journal *Frontiers in Behavioral Neuroscience*.

Debiopharm Group™ Life Sciences Award granted to CNP faculty

Grégoire Courtine received the Debiopharm Group™ Life Sciences Award 2013.



October 2013

CNP publication in Psychological Science

A new virtual reality technique that uses heart beat signals to alter bodily self-consciousness was announced. The project was developed in the Blanke Lab by Lukas Heydrich and Jane Aspell.

Campus Biotech will be the core of the Swiss neuroscience valley

The research groups of the Human Brain Project and the CNP will be based at the new Geneva Campus of EPFL and the University of Geneva.



November 2013

Welcome to our CNP-Valais team at SUVA

As part of the EPFL-Valais-Wallis initiative, the CNP announces a new partnership and important clinical and neuroengineering research at the SUVA Rehabilitation Clinic in Sion.



S. Lacour, S. Micera, J. R. Millán and G. Courtine publish this month in Science Translational Medicine

CNP faculty publishes seminal reviews on Robotics and Neuroprosthetics (vol 5, issue 210).

December 2013

Toward a deeper understanding of Spinal Cord Stimulation using computational methods

Grégoire Courtine and Silvestro Micera publish joint research on epidural electrical stimulation in spinal cord repair in the *Journal of Neuroscience*.

Olaf Blanke at the Brain Forum

Hosted in Jeddah (Saudi Arabia), the Brain Forum brought together some of the world's top inspirational thinkers and pioneers in the field of brain research and personalized healthcare.

Seminars & visits

Seminar | Multi-species studies of vestibular implants , May 2013

Prof. Daniel M Merfeld, Jenks Vestibular Physiology Laboratory, Otolaryngology, Harvard Medical School, Boston (US).

Seminar | Auditory processing in comatose patients during and after therapeutic hypothermia, June 2013

Dr. Marzia De Lucia, Lemanic Center for Biomedical Imaging, CHUV, Lausanne (CH).

Seminar | Transcranial static magnetic field stimulation over the motor and visual cortices : a new non-invasive neuromodulation strategy, June 2013

Prof. Antonio Oliviero, FENNSI, Hospital Nacional de Paraplégicos, Toledo (Spain).

Seminar | Neurological rehabilitation: from receptors to behaviour. A story told by the spinal cord and cerebellum, June 2013

Prof. Marco Molinari, Clinical Unit A and of Experimental Neurorehabilitation Lab, Santa Lucia Foundation, Rome (Italy).

Visit | Delegation from Medtronic, June 2013

Medtronic Inc. (based in Minneapolis, USA) is a world leader in medical technology and prosthetics targeting several chronic diseases such as heart failure, Parkinson's disease, urinary incontinence, obesity, chronic pain, spinal disorders, or diabetes.

Seminar | Practical non-invasive brain-machine interface system for communication and control, September 2013

Prof Kenji Kansaku, Department of Rehabilitation for Brain Functions, Research Institute of National Rehabilitation Center for Persons with Disabilities (Japan).

Seminar | Stretchy electronics that can dissolve in your body, September 2013

Prof. John Rogers, University of Illinois, Urbana Champaign (US).

Visit | Delegation from National University of Singapore & Singapore Institute for Neurotechnology , September 2013

The National University of Singapore (NUS) is a leading university in Asia and worldwide. The Singapore Institute for Neurotechnology (SINAPSE) focuses on neurotechnologies for basic science, clinical application and commercialization.

Visit | Delegation from the Korea Advanced Institute of Science and Technology, November 2013

The Korea Advanced Institute of Science and Technology (KAIST) is the largest engineering school in Korea. Its College of Life Science and Bio Engineering covers both Bio & Brain Engineering and Medical sciences.

Visit | Delegation from the University of the Chinese Academy of Sciences, November 2013

The University of the Chinese Academy of Sciences (UCAS), one of the largest university in China, is headquartered in Beijing and encompasses several campuses in more than 20 cities all over the country.

Seminar | Neuroprosthetic systems for enhancement of neuroplasticity following stroke and spinal cord injury, December 2013

Prof. Milos R. Popovic, University of Toronto (Canada).

CNP Annual Retreat, 10-11 October, Evian-les-Bains

Invited speakers

Prof Kamiar Aminian (Laboratory of Movement Analysis and Measurement, EPFL) and Prof Dimitri Van De Ville (Medical Image Processing Laboratory, EPFL).

Teaching

Students enrolled in a master program at EPFL have the possibility to obtain an inter-faculty specialization in neuroprosthetics. This “Mineur” in neuroprosthetics covers the essential courses in neurosciences and neuroengineering in the field of neuroprosthetics, including medical applications. The programme is coordinated by Prof. José del R. Millán (School of Engineering, STI) and Prof Olaf Blanke (School of Life Sciences, SV).



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